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## Public summary of opinion on orphan designation

### Ambroxol hydrochloride for the treatment of amyotrophic lateral sclerosis

On 25 May 2018, orphan designation (EU/3/18/2017) was granted by the European Commission to Spedding Research Solutions SAS, France, for ambroxol hydrochloride for the treatment of amyotrophic lateral sclerosis.

#### What is amyotrophic lateral sclerosis?

Amyotrophic lateral sclerosis (ALS) is a progressive disease of the nervous system, where nerve cells in the brain and spinal cord that control voluntary movement gradually deteriorate, causing loss of muscle function and paralysis. The exact causes are unknown but are believed to include genetic and environmental factors. The symptoms of ALS depend on which muscles weaken first, and include loss of balance, loss of control of hand and arm movement, and difficulty speaking, swallowing and breathing. ALS usually starts in mid-life and men are more likely to develop the disease than women.

ALS is a debilitating and life-threatening disease because of the gradual loss of function and its paralysing effect on muscles used for breathing, which usually leads to death from respiratory failure.

#### What is the estimated number of patients affected by the condition?

At the time of designation, ALS affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 people\*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

#### What treatments are available?

At the time of designation, riluzole and busulfan were authorised in the EU to treat ALS. Patients also received supportive treatment to relieve the symptoms of the disease, such as physiotherapy and breathing support.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with ALS. Early laboratory studies showed that the medicine could lead to

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\*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 517,400,000 (Eurostat 2018).

improvements in muscle function and survival. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

### **How is this medicine expected to work?**

Ambroxol hydrochloride is thought to modulate the activity of an enzyme called beta-glucocerebrosidase in the spinal cord. This enzyme is responsible for breaking down glycosphingolipids, which makes up cell membranes. By modulating this enzyme, the medicine is expected to help protect the cell membranes in the spinal cord and thereby improve symptoms of ALS.

### **What is the stage of development of this medicine?**

The effects of ambroxol hydrochloride have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with ambroxol hydrochloride in patients with ALS had been started.

At the time of submission, the medicine was authorised in some EU member states as expectorants for the treatment of diseases of the lungs and airways.

Ambroxol hydrochloride was not authorised anywhere in the EU for ALS or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 April 2018 recommending the granting of this designation.

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Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

## For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's [rare disease designations page](#).

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](#), a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- [European Organisation for Rare Diseases \(EURORDIS\)](#), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

## Translations of the active ingredient and indication in all official EU languages<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Ambroxol hydrochloride	Treatment of amyotrophic lateral sclerosis
Bulgarian	Амброксол хидрохлорид	Лечение на амиотрофична латерална склероза
Croatian	Ambroksol hidroklorid	Liječenje amiotrofične lateralne skleroze
Czech	Ambroxol-hydrochlorid	Léčba amyotrofické laterální sklerózy (ALS)
Danish	Ambroxolhydrochlorid	Behandling af amyotrofisk lateralsklerose
Dutch	Ambroxol hydrochloride	Behandeling van amyotrofe lateraalsclerose
Estonian	Ambroksoolvesinikkloriid	Amüotroofilise lateraalskleroosi ravi
Finnish	Ambroksolihydrokloridi	Amyotrofisen lateraalskleroosin hoito
French	Chlorhydrate d'ambroxol	Traitement de la sclérose latérale amyotrophique
German	Ambroxol hydrochlorid	Behandlung der amyotrophen Lateralsklerose
Greek	Αμβροξόλη υδροχλωρική	Θεραπεία πλάγιας μυοατροφικής σκλήρυνσης
Hungarian	Ambroxol hidroklorid	Amyotrophiás lateral sclerosis kezelése
Italian	Ambroxolo cloridrato	Trattamento della sclerosi laterale amiotrofica
Latvian	Ambroksola hidrohlorīds	Amiotrofiskās laterālās sklerozes ārstēšana
Lithuanian	Ambroksolio hidrochloridas	Šoninės amiotrofinės sklerozės gydymas
Maltese	Idroklorur ambrossoliku	Kura tas-sklerosi laterali amjotrofika
Polish	Chlorowodorek ambroksolu	Leczenie stwardnienia bocznego zanikowego
Portuguese	Cloridrato de ambroxol	Tratamento da esclerose lateral amiotrófica
Romanian	Clorhidrat de ambroxol	Tratamentul sclerozei laterale amiotrofice
Slovak	Ambroxol hydrochlorid	Liečba amyotrofickéj laterálnej sklerózy
Slovenian	Ambroksol hidroklorid	Zdravljenje amiotrofične lateralne skleroze
Spanish	Cloridrato de Ambroxol	Tratamiento de la esclerosis lateral amiotrófica
Swedish	Ambroxolhydroklorid	Behandling av amyotrofisk lateralskleros
Norwegian	Ambroksol hydroklorid	Behandling av amyotrofisk lateralsklerose
Icelandic	Ambroxól hýdróklóríð	Meðferð við blandaðri hreyfitaugahrönnun

<sup>1</sup> At the time of designation